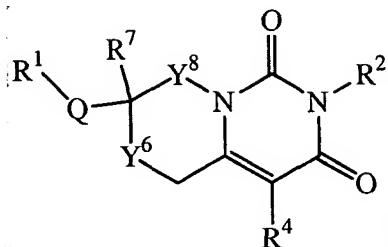


CLAIMS

What is claimed is:

5

1. A compound of Formula I



I

or a pharmaceutically acceptable salt thereof,

wherein:

10 R^1 is independently selected from:

C_5 or C_6 cycloalkyl-(C_1 - C_8 alkylényl);

Substituted C_5 or C_6 cycloalkyl-(C_1 - C_8 alkylényl);

C_8 - C_{10} bicycloalkyl-(C_1 - C_8 alkylényl);

Substituted C_8 - C_{10} bicycloalkyl-(C_1 - C_8 alkylényl);

15 5- or 6-membered heterocycloalkyl-(C_1 - C_8 alkylényl);

Substituted 5- or 6-membered heterocycloalkyl-(C_1 - C_8 alkylényl);

8- to 10-membered heterobicycloalkyl-(C_1 - C_8 alkylényl);

Substituted 8- to 10-membered heterobicycloalkyl-(C_1 - C_8 alkylényl);

Phenyl-(C_1 - C_8 alkylényl);

20 Substituted phenyl-(C_1 - C_8 alkylényl);

Naphthyl-(C_1 - C_8 alkylényl);

Substituted naphthyl-(C_1 - C_8 alkylényl);

5- or 6-membered heteroaryl-(C_1 - C_8 alkylényl);

Substituted 5- or 6-membered heteroaryl-(C_1 - C_8 alkylényl);

25 8- to 10-membered heterobiaryl-(C_1 - C_8 alkylényl);

Substituted 8- to 10-membered heterobiaryl-(C_1 - C_8 alkylényl);

Phenyl;

Substituted phenyl;

Naphthyl;

Substituted naphthyl;
5- or 6-membered heteroaryl;
Substituted 5- or 6-membered heteroaryl;
8- to 10-membered heterobiaryl; and
5 Substituted 8- to 10-membered heterobiaryl;

R^2 is independently selected from:

H;
 C_1 - C_6 alkyl;
Phenyl-(C_1 - C_8 alkylene);
10 Substituted phenyl-(C_1 - C_8 alkylene);
Naphthyl-(C_1 - C_8 alkylene);
Substituted naphthyl-(C_1 - C_8 alkylene);
5- or 6-membered heteroaryl-(C_1 - C_8 alkylene);
Substituted 5- or 6-membered heteroaryl-(C_1 - C_8 alkylene);
15 8- to 10-membered heterobiaryl-(C_1 - C_8 alkylene);
Substituted 8- to 10-membered heterobiaryl-(C_1 - C_8 alkylene);
Phenyl-O-(C_1 - C_8 alkylene);
Substituted phenyl-O-(C_1 - C_8 alkylene);
Phenyl-S-(C_1 - C_8 alkylene);
20 Substituted phenyl-S-(C_1 - C_8 alkylene);
Phenyl-S(O)-(C_1 - C_8 alkylene);
Substituted phenyl-S(O)-(C_1 - C_8 alkylene);
Phenyl-S(O)₂-(C_1 - C_8 alkylene); and
Substituted phenyl-S(O)₂-(C_1 - C_8 alkylene);

25 Each substituted R^1 and R^2 group contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom, independently selected from:

C_1 - C_6 alkyl;
CN;
 CF_3 ;
30 HO;
(C_1 - C_6 alkyl)-O;
(C_1 - C_6 alkyl)-S(O)₂;
H₂N;

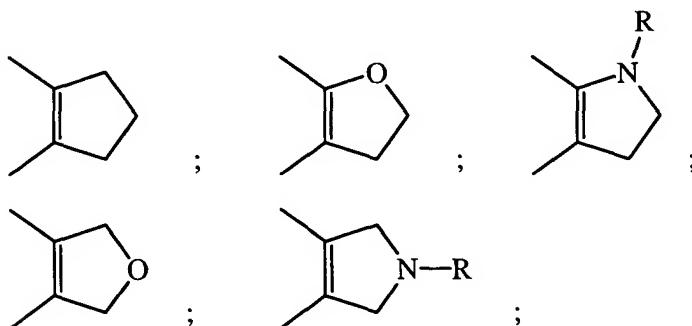
(C₁-C₆ alkyl)-N(H);
(C₁-C₆ alkyl)₂-N;
(C₁-C₆ alkyl)-C(O)O-(C₁-C₈ alkyleneyl)_m;
(C₁-C₆ alkyl)-C(O)O-(1- to 8-membered heteroalkyleneyl)_m;
5 (C₁-C₆ alkyl)-C(O)N(H)-(C₁-C₈ alkyleneyl)_m;
(C₁-C₆ alkyl)-C(O)N(H)-(1- to 8-membered heteroalkyleneyl)_m;
H₂NS(O)₂-(C₁-C₈ alkyleneyl);
(C₁-C₆ alkyl)-N(H)S(O)₂-(C₁-C₈ alkyleneyl)_m;
(C₁-C₆ alkyl)₂NS(O)₂-(C₁-C₈ alkyleneyl)_m;
10 3- to 6-membered heterocycloalkyl-(G)_m;
Substituted 3- to 6-membered heterocycloalkyl-(G)_m;
5- or 6-membered heteroaryl-(G)_m;
Substituted 5- or 6-membered heteroaryl-(G)_m;
(C₁-C₆ alkyl)-S(O)₂-N(H)-C(O)-(C₁-C₈ alkyleneyl)_m; and
15 (C₁-C₆ alkyl)-C(O)-N(H)-S(O)₂-(C₁-C₈ alkyleneyl)_m;

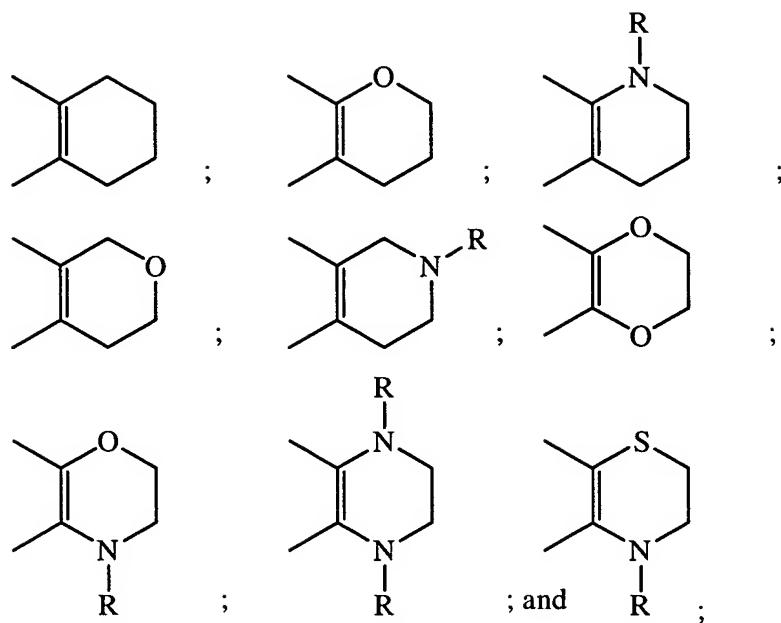
wherein each substituent on a carbon atom may further be independently selected from:

Halo; and

HO₂C;

20 wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;
wherein two adjacent, substantially sp² carbon atoms may be taken together with a diradical substituent to form a cyclic diradical selected from:





R is H or C₁-C₆ alkyl;

5 G is CH₂; O, S, S(O); or S(O)₂;

m is an integer of 0 or 1;

R⁷ is independently selected from the groups:

H;

CH₃;

10 CH₃O;

CH=CH₂;

HO;

CF₃;

CN;

15 HC(O);

CH₃C(O);

HC(NOH);

H₂N;

(CH₃)-N(H);

20 (CH₃)₂-N;

H₂NC(O);

(CH₃)-N(H)C(O);

(CH₃)₂-NC(O);

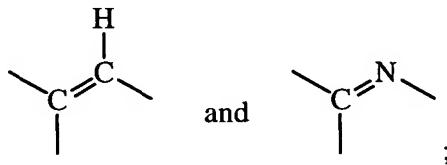
halo; and

CO_2H ;

Y^6 and Y^8 are each independently CH_2 , $\text{C}(\text{O})$, O , S , $\text{S}(\text{O})$, $\text{S}(\text{O})_2$, or $\text{N}(\text{R}^5)$; or

R^7 and Y^8 may be taken together with the carbon atom to which they are both

5 attached to form a group selected from:



R^4 and R^5 are each independently selected from the groups:

H ;

CH_3 ;

10 CH_3O ;

$\text{CH}=\text{CH}_2$;

HO ;

CF_3 ;

CN ;

15 $\text{HC}(\text{O})$;

$\text{CH}_3\text{C}(\text{O})$;

$\text{HC}(\text{NOH})$;

H_2N ;

$(\text{CH}_3)\text{-N}(\text{H})$;

20 $(\text{CH}_3)_2\text{-N}$;

$\text{H}_2\text{NC}(\text{O})$;

$(\text{CH}_3)\text{-N}(\text{H})\text{C}(\text{O})$; and

$(\text{CH}_3)_2\text{-NC}(\text{O})$;

Q is selected from:

25 $\text{OC}(\text{O})$;

$\text{CH}(\text{R}^6)\text{C}(\text{O})$;

$\text{OC}(\text{NR}^6)$;

$\text{CH}(\text{R}^6)\text{C}(\text{NR}^6)$;

$\text{N}(\text{R}^6)\text{C}(\text{O})$;

30 $\text{N}(\text{R}^6)\text{C}(\text{S})$;

O, 1 S, 1 S(O), 1 S(O)₂, 1 N, 4 N(H), and 4 N(C₁-C₆ alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond, and wherein the heterobicycloalkyl is a 5,5-fused, 6,5-fused, or 6,6-fused bicyclic ring, respectively,

5 wherein each heterocycloalkyl is a ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)₂, 1 N, 4 N(H), and 4 N(C₁-C₆ alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

10 wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C₁-C₆ alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms and 1 or 2 heteroatoms independently selected from N, N(H), and N(C₁-C₆ alkyl), and 5- and 6-membered heteroaryl are monocyclic rings;

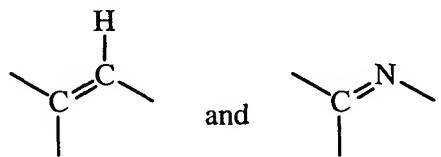
15 wherein each heterobiaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C₁-C₆ alkyl), and 4 N, and where the 8-, 9-, and 10-membered heterobiaryl are 5,5-fused, 6,5-fused, and 6,6-fused bicyclic rings, respectively, and wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other;

20 wherein with any (C₁-C₆ alkyl)₂-N group, the C₁-C₆ alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl; and

25 wherein each group and each substituent recited above is independently selected.

30 2. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein each of Y⁶ and Y⁸ is independently CH₂ or S(O)₂.

3. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein R⁷ and Y⁸ are taken together with the carbon atom to which they are both attached to form a group selected from:



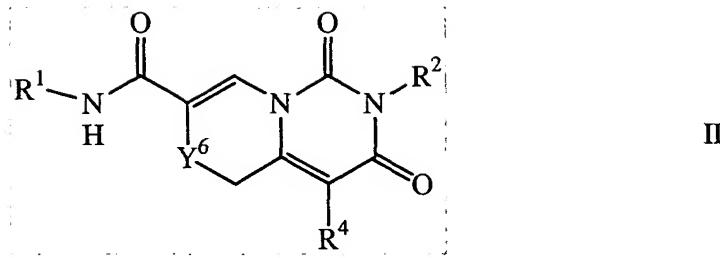
5

4. The compound according to Claim 1, wherein Q is C≡C.

5. The compound according to Claim 1, wherein Q is N(R⁶)C(O).

10 6. The compound according to any one of Claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein R¹ is independently selected from:
Phenyl-(C₁-C₈ alkylenyl);
Substituted phenyl-(C₁-C₈ alkylenyl);
15 5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);
Substituted 5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);
8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl); and
Substituted 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl); and
R² is independently selected from:
20 Phenyl-(C₁-C₈ alkylenyl)_m;
Substituted phenyl-(C₁-C₈ alkylenyl)_m;
5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl)_m;
Substituted 5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl)_m;
8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl)_m; and
25 Substituted 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl)_m;
wherein m is an integer of 0 or 1; and
wherein each group and each substituent is independently selected.

7. The compound according to Claim 1 of Formula II



8. The compound according to Claim 7 selected from:

7-(3,5-Difluoro-4-hydroxy-benzyl)-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-

5 2H-pyrazino[1,2-c]pyrimidine-3-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide;

7-Benzyl-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-2H-pyrazino[1,2-c]pyrimidine-3-carboxylic acid 3-methoxy-benzylamide;

10 7-(3,4-Difluoro-benzyl)-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-2H-pyrazino[1,2-c]pyrimidine-3-carboxylic acid (pyridin-4-ylmethyl)-amide;

7-Benzyl-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-2H-pyrazino[1,2-c]pyrimidine-3-carboxylic acid (pyridin-4-ylmethyl)-amide;

15 7-Benzyl-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-2H-pyrazino[1,2-c]pyrimidine-3-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide;

7-(3,4-Difluoro-benzyl)-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-2H-pyrazino[1,2-c]pyrimidine-3-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide;

20 7-[4-(3-Ethyl-ureido)-benzyl]-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-2H-pyrazino[1,2-c]pyrimidine-3-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide;

7-(3,4-Difluoro-benzyl)-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-2H-pyrazino[1,2-c]pyrimidine-3-carboxylic acid 4-fluoro-

25 benzylamide;

6-Benzyl-8-methyl-5,7-dioxo-1,2,4a,5,6,7-hexahydro-2,6-naphthyridine-3-carboxylic acid 4-fluoro-benzylamide;

7-(4-Cyano-benzyl)-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-2H-pyrazino[1,2-c]pyrimidine-3-carboxylic acid 4-fluoro-benzylamide;

7-(3,5-Difluoro-4-hydroxy-benzyl)-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-5-pyrimido[6,1-c][1,4]oxazine-3-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide;

7-Benzyl-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-pyrimido[6,1-c][1,4]oxazine-3-carboxylic acid 3-methoxy-benzylamide;

7-(3,4-Difluoro-benzyl)-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-10-pyrimido[6,1-c][1,4]oxazine-3-carboxylic acid (pyridin-4-ylmethyl)-amide;

7-Benzyl-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-pyrimido[6,1-c][1,4]oxazine-3-carboxylic acid (pyridin-4-ylmethyl)-amide;

7-Benzyl-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-pyrimido[6,1-c][1,4]oxazine-3-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide;

7-(3,4-Difluoro-benzyl)-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-pyrimido[6,1-c][1,4]oxazine-3-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide;

7-[4-(3-Ethyl-ureido)-benzyl]-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-20-pyrimido[6,1-c][1,4]oxazine-3-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide;

7-(3,4-Difluoro-benzyl)-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-pyrimido[6,1-c][1,4]oxazine-3-carboxylic acid 4-fluoro-benzylamide;

6-Benzyl-8-methyl-5,7-dioxo-4a,5,6,7-tetrahydro-1H-pyrano[4,3-c]pyridine-3-carboxylic acid 4-fluoro-benzylamide;

7-(4-Cyano-benzyl)-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-pyrimido[6,1-c][1,4]oxazine-3-carboxylic acid 4-fluoro-benzylamide;

7-(3,5-Difluoro-4-hydroxy-benzyl)-9-methyl-2,2,6,8-tetraoxo-1,6,7,8-tetrahydro-2H-2^f-pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid 30-(2-methoxy-pyridin-4-ylmethyl)-amide;

7-Benzyl-9-methyl-2,2,6,8-tetraoxo-1,6,7,8-tetrahydro-2H-2*t*⁶-
5 pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid 3-methoxy-
benzylamide;
7-(3,4-Difluoro-benzyl)-9-methyl-2,2,6,8-tetraoxo-1,6,7,8-tetrahydro-2H-
10 2*t*⁶-pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid (pyridin-4-
ylmethyl)-amide;
7-Benzyl-9-methyl-2,2,6,8-tetraoxo-1,6,7,8-tetrahydro-2H-2*t*⁶-
15 pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid (pyridin-4-
ylmethyl)-amide;
7-(3,4-Difluoro-benzyl)-9-methyl-2,2,6,8-tetraoxo-1,6,7,8-tetrahydro-2H-
20 2*t*⁶-pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid (2-methoxy-
benzyl)-amide;
7-[4-(3-Ethyl-ureido)-benzyl]-9-methyl-2,2,6,8-tetraoxo-1,6,7,8-
25 tetrahydro-2H-2*t*⁶-pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid
(2-methoxy-pyridin-4-ylmethyl)-amide;
7-(3,4-Difluoro-benzyl)-9-methyl-2,2,6,8-tetraoxo-1,6,7,8-tetrahydro-2H-
30 2*t*⁶-pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid 4-fluoro-
benzylamide;
6-Benzyl-8-methyl-2,2,5,7-tetraoxo-1,2,4a,5,6,7-hexahydro-2*t*⁶-
thiopyrano[4,3-c]pyridine-3-carboxylic acid 4-fluoro-benzylamide;
and
25 7-(4-Cyano-benzyl)-9-methyl-2,2,6,8-tetraoxo-1,6,7,8-tetrahydro-2H-2*t*⁶-
pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid 4-fluoro-
benzylamide;
or a pharmaceutically acceptable salt thereof.

30 9. The compound according to Claim 7 selected from:
7-(3,5-Difluoro-4-hydroxy-benzyl)-2-hydroxy-9-methyl-6,8-dioxo-1,6,7,8-
tetrahydro-2H-2*t*⁴-pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid
(2-methoxy-pyridin-4-ylmethyl)-amide;

7-Benzyl-2-hydroxy-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-2H-2*t*⁴-
pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid 3-methoxy-
benzylamide;

7-(3,4-Difluoro-benzyl)-2-hydroxy-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-
2H-2*t*⁴-pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid (pyridin-4-
ylmethyl)-amide;

7-Benzyl-2-hydroxy-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-2H-2*t*⁴-
pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid (pyridin-4-
ylmethyl)-amide;

7-Benzyl-2-hydroxy-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-2H-2*t*⁴-
pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid (2-methoxy-
pyridin-4-ylmethyl)-amide;

7-(3,4-Difluoro-benzyl)-2-hydroxy-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-
2H-2*t*⁴-pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid (2-methoxy-
pyridin-4-ylmethyl)-amide;

7-[4-(3-Ethyl-ureido)-benzyl]-2-hydroxy-9-methyl-6,8-dioxo-1,6,7,8-
tetrahydro-2H-2*t*⁴-pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid
(2-methoxy-pyridin-4-ylmethyl)-amide;

7-(3,4-Difluoro-benzyl)-2-hydroxy-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-
2H-2*t*⁴-pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid 4-fluoro-
benzylamide;

6-Benzyl-2-hydroxy-8-methyl-5,7-dioxo-1,2,4a,5,6,7-hexahydro-2*t*⁴-
thiopyrano[4,3-c]pyridine-3-carboxylic acid 4-fluoro-benzylamide;

7-(4-Cyano-benzyl)-2-hydroxy-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-2H-
2*t*⁴-pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid 4-fluoro-
benzylamide;

7-(3,5-Difluoro-4-hydroxy-benzyl)-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-
pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid (2-methoxy-
pyridin-4-ylmethyl)-amide;

7-Benzyl-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-pyrimido[6,1-
c][1,4]thiazine-3-carboxylic acid 3-methoxy-benzylamide;

7-(3,4-Difluoro-benzyl)-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-
pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid (pyridin-4-
ylmethyl)-amide;
7-Benzyl-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-pyrimido[6,1-
5 c][1,4]thiazine-3-carboxylic acid (pyridin-4-ylmethyl)-amide;
7-Benzyl-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-pyrimido[6,1-
c][1,4]thiazine-3-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-
amide;
7-(3,4-Difluoro-benzyl)-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-
10 pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid (2-methoxy-
pyridin-4-ylmethyl)-amide;
7-[4-(3-Ethyl-ureido)-benzyl]-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-
pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid (2-methoxy-
pyridin-4-ylmethyl)-amide;
15 7-(3,4-Difluoro-benzyl)-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-
pyrimido[6,1-c][1,4]thiazine-3-carboxylic acid 4-fluoro-
benzylamide;
6-Benzyl-8-methyl-5,7-dioxo-4a,5,6,7-tetrahydro-1H-thiopyrano[4,3-
c]pyridine-3-carboxylic acid 4-fluoro-benzylamide; and
20 7-(4-Cyano-benzyl)-9-methyl-6,8-dioxo-1,6,7,8-tetrahydro-pyrimido[6,1-
c][1,4]thiazine-3-carboxylic acid 4-fluoro-benzylamide;
or a pharmaceutically acceptable salt thereof.

25 10. A pharmaceutical composition, comprising a compound of Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

11. The pharmaceutical composition according to Claim 10, comprising a compound according to Claim 8 or 9, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

30 12. A method for treating osteoarthritis or rheumatoid arthritis, comprising administering to a patient suffering from osteoarthritis or rheumatoid arthritis a

nontoxic effective amount of a compound of Claim 1, or a pharmaceutically acceptable salt thereof.

13. The method according to Claim 12 wherein the compound of Claim 1 is a
5 compound of Claim 8 or 9.